Analysis of Long-Term Electrocardiographic Data in a Rabbit Model of Heart Failure

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Abstract-**The goal of this research is to explore techniques with which long-term physiologic time-series data can be analyzed, so that relevant changes in physiological signals, particularly the electrocardiogram signal, can be captured, processed, quantified and stored. A new experimental model was developed such that the electrocardiogram can be monitored continuously over thirteen weeks. Cardiotoxicity was progressively induced with doxorubicin in a rabbit model, and electrocardiographic progressions from normal state to diseased state were continuously tracked. Automated methods for analyzing the data were developed to manage and control the extensive electrocardiogram dataset. A significant challenge to this work is the sheer mass of data. This experiment generated 180 megabytes per day per rabbit, totaling around 66 gigabytes for the entire study. Classical ECG parameters significant for the evaluation of heart rate variability were calculated by computer for the entire period of the recordings, and visualized with several different methods.**
Keywords - **Long-term recordings, heart rate variability, rabbit, electrocardiogram**

I. Introduction

The rapid advances in computing power, miniature radio-transmitters, and the relative inexpensiveness of data storage, makes it now possible to perform long-term physiologic monitoring where the data is recorded for many months, even years, to document physiologic changes. Despite these advances, little or no work of this type has been performed in the biomedical area to discover insight into physiologic mechanisms and disease. Tools and methods for handling and processing must be developed and utilized, so that significant and relevant changes in physiological signals can be captured, analyzed, quantified and stored. In comparison with short-term recordings, long–term recordings are very large, and complex data sets.

The quality of the long-term recordings, provided by the most recent technology, opens new doors for the study and prediction of heart diseases. This is especially important because one to two million adults are affected in the United States by heart failure with 200,000 deaths annually [1,2]. In addition, 30-50% of these deaths are sudden and have been attributed to ventricular tachyarrhythmias, bradycardia, and electro-mechanical dissociation [1,2]. Longitudinal tracking of electrocardiographic (ECG) changes could impact understanding of the disease and the changes that occur over time as the disease develops.

A *new* experimental model has been developed such that the electrocardiogram can be monitored *continuously*, that is, a 1000 samples per second, over thirteen weeks. In this model cardiotoxicity was progressively induced with doxorubicin in a rabbit model [3], and the ECG was continuously tracked. A significant challenge to this work is the sheer mass of data. This experiment generated 180 megabytes per day per rabbit, totaling 66 gigabytes for the study reported in this paper. For five weeks, classical ECG parameters were calculated by computer and monitored before and during the development of heart disease. Unique, automated methods for analyzing the data were developed to manage and control the extensive electrocardiogram dataset.

II. Methods

Three animals were used for this study. Two received weekly injections (1 mg/ml) of doxurubin [3]. One was a control receiving saline injections (R710V). These animals were outfitted with implantable telemetry systems which recorded the electrocardiogram (Datasciences, Intl.). All three animals were monitored for fourteen weeks. One animal died spontaneously of heart failure (R735W). The second animal was sacrificed after ten weeks of injections due to excessive pain and discomfort from heart failure (R733W). The control animal had no complications.

The first animal was placed in the lead II configuration. This lead placement was subject to motion artifact due to its nearness to the limbs. The second animal was placed in a modified lead position, between the manubrium sternum and xiphoid process [4]. This configuration was better during motion. The third animal had a similar surface lead placement. In addition, the implantable monitor also recorded a second intracardiac channel, a bipolar electrode lead placed with fluoroscopy in the right side of the ventricle through the jugular vein. The intracardiac channel had no artifact due to motion and is optimal for calculation of parameters related to RR variability.

The electrocardiogram data was continuously monitored at 1000 samples per second and was telemetered through radiofrequency to a receiver in the cage which is connected to a personal computer where it is stored. Custom software was developed which automatically downloaded the data daily from the PC to a dataserver over the network. In addition, custom software converted the data from the manufacturer's format to a readable format. Each datafile was 8 megabytes which holds approximately 1 hour of data for one channel. This results in approximately 180 megabytes of data generated per day.

Custom software was developed which performs noise rejection based on the RR interval [5] and then computes eleven standard heart rate variability (HRV) parameters, including time-domain measures like standard deviation, and frequency domain measures [6]. These parameters were

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Abstract

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3

calculated continuously for every usable five-minute segment.

Parameters relevant to HRV were computed for every 5-minute segment ECG and stored each in a vector of length 288 (one day has 288 5-minute segments). Data was averaged hourly and weekly. A single vector of length 24 (hours) was obtained for one week. These vectors were obtained for each rabbit, for all parameters, and 5 weeks were plotted: week –1, the first week prior to the injection, weeks 3, 5, 7 after the first injection, and week 9 for rabbits R710V and R733W and week 8 for rabbit R735W, since this rabbit died before the end of week 9. Comparisons were made within an animal (Fig. 1) and across animals (Fig. 2).

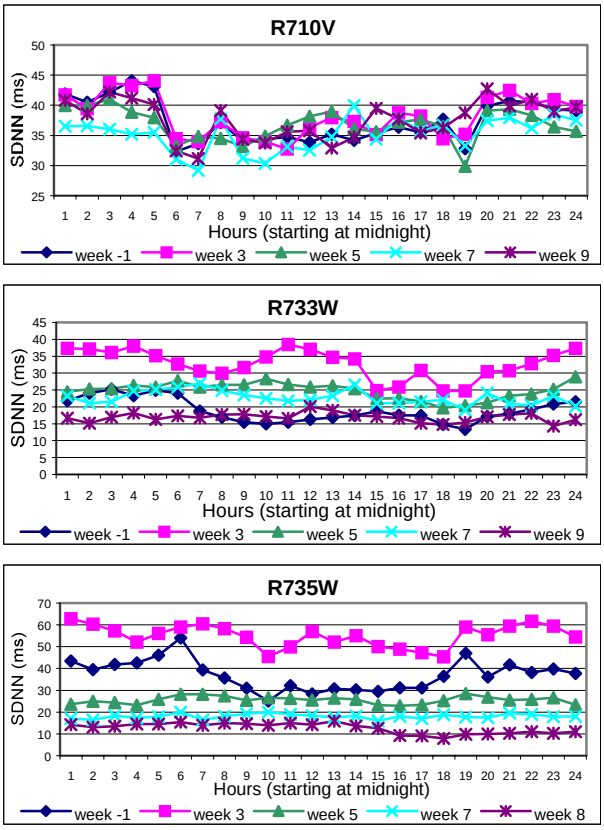
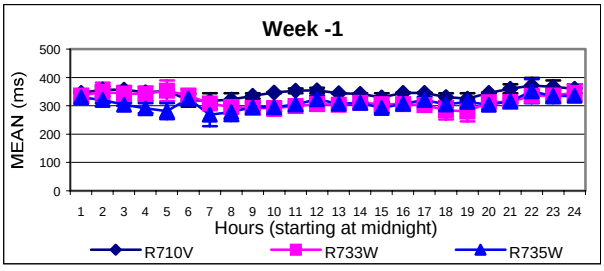


Fig. 1. Standard deviation of RR intervals in 24-hour period of week -1, 3, 5, and 9 (for R710V and R733W) and 8 (for R735W)



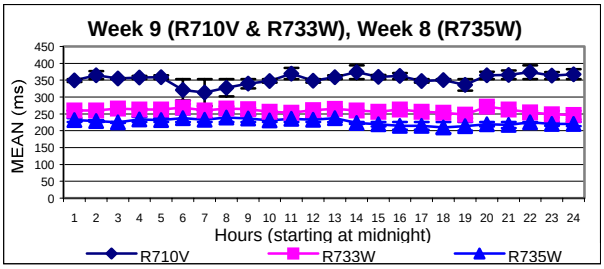


Fig. 2. Mean of RR intervals of R710V, R733W, and R735W at the week -1 (top), and week 9 (bottom) for R710V and R733W and week 8 for R735W

In addition, day and night interactions were studied by averaging over the day and night across each week (Fig. 3). Lastly, scatter plots were generated which used *every* 5-minute segment within each week (Fig. 4).

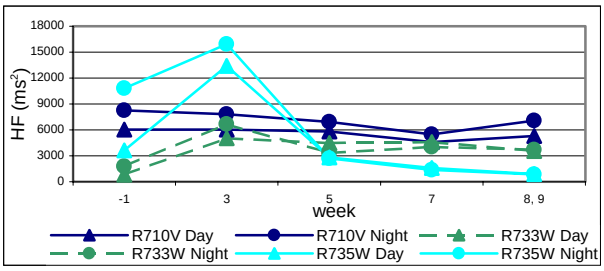


Fig. 3. Variation of high frequency (HF) between night and day

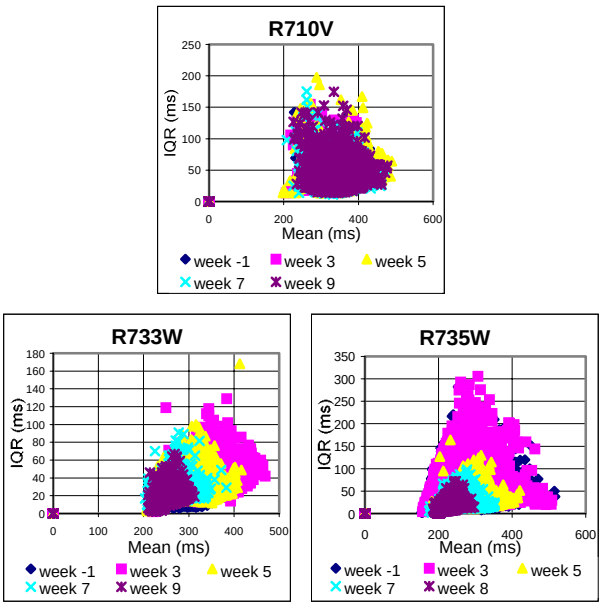


Fig. 4. 2D plots between interquartile range of RR intervals and mean of RR intervals

III. Results

The method was successful in continuously collecting electrocardiographic data in animals during the development of heart failure. Data were stored for fourteen weeks with minimal loss of data during injections and cage cleanings. Intracardiac signals were the least susceptible to noise. Analyses for five weeks are shown in this paper.

The results show the evolution of heart rate variability parameters during the progression of heart failure. In case of the control rabbit, R710V, which was injected with saline, the variation of all eleven parameters was within a very small range of values. For rabbits R733W and R735W all HRV parameters presented an increase in week 3, with a higher variation compared with week–1, and then a decrease with almost no variations by week 9 (Figures 1 and 2). In addition, there is little day/night difference at week 9 for the heart failure animals (Figure 3). Lastly, the scatter plots demonstrate the loss of variability over the course of the study (Figure 4). More animals will need to be studied to be able to generalize information regarding the heart failure model.

IV. Conclusion

The goal of this research is to explore techniques with which long-term physiologic time-series data can be analyzed. For the first time, long-term studies, particularly electrocardiographic progressions from normal state to diseased state have been continuously tracked. In this paper, a *new* experimental model was developed such that the electrocardiogram can be monitored *continuously*, that is, a 1000 samples per second, over thirteen weeks. In this model cardiotoxicity was progressively induced with doxorubicin in a rabbit model, and the ECG was continuously tracked. A significant challenge to this work is the sheer mass of data. This experiment generated 180 megabytes per day per rabbit, totaling 66 gigabytes for the study. Techniques were shown to summarize and present this massive amount of data.

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